REMARKS

In the specification, the paragraphs and tables containing a mistranslated term "partially alphanized starch" have been substituted with paragraphs and tables containing the correct translation of the Japanese term "partly pregelatinized starch." The error in translation occurred at the time the PCT application entered the national phase in the U.S.

The term used in the Japanese PCT application is the correct technical term (see underlined Japanese word in the Japanese PCT application reciting the Japanese, Appendix A). A copy of the relevant pages of Japanese Pharmaceutical Excipients in Japanese, which also shows that the Japanese term erroneously translated as "partially alphanized starch" means "partly pregelatinized starch" (Appendix A). To expedite prosecution and if examiner so requests, applicants are prepared to submit a sworn statement from a translator to confirm that a mistake was made during translation from the priority document written in Japanese. Therefore, applicants submit that these amendments do not introduce new matter and their entry is respectfully requested.

Claims 1-18 have been deleted and new claims 19-46 are being submitted.

Claim 19 is directed to a surface modified powder, with a flowability of at maximum 42° as measured using angle of repose. Support for adding the angle of repose to the claim can be found in the descriptions of the present specification at page 12, line 25 to page 13, line 14, and at page 16, lines 1 to 20. Further support can be found in Examples 1 through 9, which show that the surface modified powder was prepared by thoroughly blending the active agent with the surface modifying material by a high speed mixer without the use of any solvent such as water. Also, Examples 1 and 2 show that the surface modified powder was prepared by thoroughly blending the active agent with the surface modifying material by a high speed mixer without the use of any solvent, such as water to give the surface modified powder, of which the angle of repose was at most 42°.

Claim 20 is directed to the powder of claim 19 further comprising a diluent and claim 21 is directed to the powder of claim 19 additionally comprising disintegrant. Support for the additional use of diluents can be found, for example, on page 11, 1st full par. Support for the

additional use of disintegrants can be found, for example, on page 17, 2nd full par.

Claims 23-27 correspond to the originally submitted claims 2-6 and further define the types of surface modifying materials in these embodiments of the invention. Examples of the surface modifying materials useful according to the present invention are described in detail on page 12, 1st full par.

Claim 28 corresponds to the originally submitted claim 7 and is directed to the tablets optionally comprising specific diluents.

Claim 29 corresponds to the originally submitted claim 9 and defines active agents of this embodiment.

The method of claim 30 corresponds to the originally submitted method of claim 10.

Claims 31 and 32 are directed to a method which specifically uses a high speed mixer to blend the powder. These claims are supported, for example, in Examples 1 through 9. Particularly useful high speed mixers are listed on page 13, lines 3-14.

Claim 33 is directed to the optional use of diluent in the method of claim 29.

Claims 34-36 corresponds to the originally submitted claims 11-14

Claims 37-46 are directed to method of producing a disintegrating tablet and correspond to the originally submitted claims 14 and 18. Claim 40 is directed to the method wherein at least one member selected from finely titanium oxide, talc and the like is further added. Support for claim 40 can be found in the specification, for example, on page 13, line 23 to page 14, line 28.

Claim 46 is directed to the situation where the optional diluent is not present. These amended claims do not constitute new matter and their entry is requested.

Turning now to the specific rejections by the examiner.

Claims 1, 2, 6, 7, 10, 14, 17, and 18 were rejected under 35 USC § 112, 2nd par. as being indefinite.

Applicants have cancelled claims 1-18 and submit new claims 19-46, wherein applicants have address examiners' comments concerning wordiness and interpretation difficulties. Applicants submit that this has obviated the rejection.

Claims 15 and 16 were rejected under 35 USC § 101 as being improper process claims. Applicants have cancelled claims 15 and 16, which obviates the rejection.

Claims 1-4, 7, 9-14, 17 and 18 were rejected under 35 USC § 102(b) as being anticipated

by GB 1,480,175.

Applicants disagree. The characteristic of the present invention resides in the surface modified powder which is obtained by blending the active agent with the surface modifying material thoroughly to the extent that the flowability of the obtained surface modified powder becomes at most 42° when measured by the angle of repose. One way of achieving this is by the use of a high speed mixer. The invention is based upon a discovery that high flowability can be achieved without the use of any solvent such as water. (See e.g., claim 46.) Therefore, the claimed surface modified powder enables direct tableting and provides material to prepare an excellent fast disintegrating tablet.

Unlike the present invention which provides for a highly flowable powder even without addition of solvent, GB 1,480,175 describes coated tablets wherein the pharmacologically active ingredient must be mixed with maltose. The tablets are prepared by mixing the pharmacologically active ingredient with maltose and then compressing the mixture into tablets and consequently coating the tablets. The method of GB 1,480,175 only enables the direct compression of the mixture into the tablet by the use of maltose, as described in GB 1,480,175 Reference 1 at page 2, the left column, lines 16 to 28. In other words, the characteristic of the invention resides entirely in the use of maltose. Moreover, when one looks at such methodology, it is clear that it does not teach or suggest a powder having a flowability of at most 42° in terms of an angle of repose.

In light of the above, the rejection under 35 USC § 102(b) over GB 1,480,175, should be withdrawn.

Claims 1-14, 17 and 18 were further rejected under 35 USC § 102(b) as being anticipated by JP 10114655. Applicants disagree.

JP 10114655 describes a pharmaceutical preparation comprising a medicine, a neutral or basic additive and a disintegrating agent, and further describes that such a preparation is rapidly disintegrable. However, unlike the present invention which teaches a powder made without the use of solvents, as required by, for example, claims 45 and 46, JP 10114655 teaches no more than a conventional method for formulating a solid pharmaceutical preparation, wherein water is used as a solvent to prepare a granulated product. Indeed, all of the Examples describe a conventional manner for formulating a tablet by mixing and granulating the medicine, additive

and disintegrating agent in the presence of water in a mixing granulator and compressing the granulated product to formulate the tablet.

Similarly, unlike the powder of the present invention, it would not have a flowability as required by the claims. Therefore, JP 10114655 neither teaches nor suggests the surface modified powder of the present invention which is obtained by thoroughly blending the active agent with the surface modifying material by the high speed mixer without the use of any solvent such as water. Therefore, the rejection under 35 USC § 102(b) over JP 10114655 should be withdrawn.

Claims 1-14, 17 and 18 were rejected under 35 USC § 103(a) as being unpatentable over GB 1,480,175. The examiner contends that the citation to the angle of repose does not allow one to distinguish the present invention from the prior art.

Applicants disagree. Claim 19 is directed to a surface modified powder, with a flowability of at maximum 42° as measured using angle of repose. Angle of repose is a well known term in the art of pharmaceutical industry and defines the maximum angle at which a mass or pile of unconsolidated solid material can remain stable. (See, e.g., Remington: The Science and Practice of Pharmacy by Alfonso R. Gennaro (Editor), A. L. Gennaro, Lippincott, Williams & Wilkins; (December 15, 2000) ISBN: 0683306472, p. 691). Flow properties of solid pharmaceutical compositions are usually determined by measuring the angle of repose. Anyone skilled in the art would readily appreciate that an angle of repose of at most at 42° is an indication of a highly flowable material. Such a material is not suggested by the prior art. Further, the present invention provides a powder which is highly flowable because it is thoroughly blended with surface modifying material and this can even be accomplished without addition of solvents, which are commonly used to increase the solid material flow in the prior art including GB 1,480,175, which distinctly requires the use of maltose as a solvent.

In view of the foregoing, applicant respectfully submits that all claims are in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the PTO is authorized to charge Nixon Peabody deposit account No. 50-0850.

Respectfully submitted,

Date: 5/12/03

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Japanese PCT application

APPENDIX A p. 1/4
09/936,558
Resp. to OA 2/10/03

１０．薬効成分又は薬効成分と希釈剤からなる表面改質用粉体を、表面改質基材と混合して表面改質し、直接打錠可能な流動性を有する請求項１から９のいずれかに記載の薬効成分含有表面改質粉体を製造する、薬効成分含有表面改質粉体の製造方法。

１１．請求項１から９のいずれかに記載の薬効成分含有表面改質粉体と、崩壊剤を混合して、直接打錠することによって得た速崩壊型錠剤。

Claim 12

１２．崩壊剤として、部分アルファー化デンプン又はクロスポビドンを用いる請求項１１記載の速崩壊型錠剤。

Claim 13

１３．部分アルファー化デンプン又はクロスポビドンを１０～６０重量%含む請求項１２記載の速崩壊型錠剤。

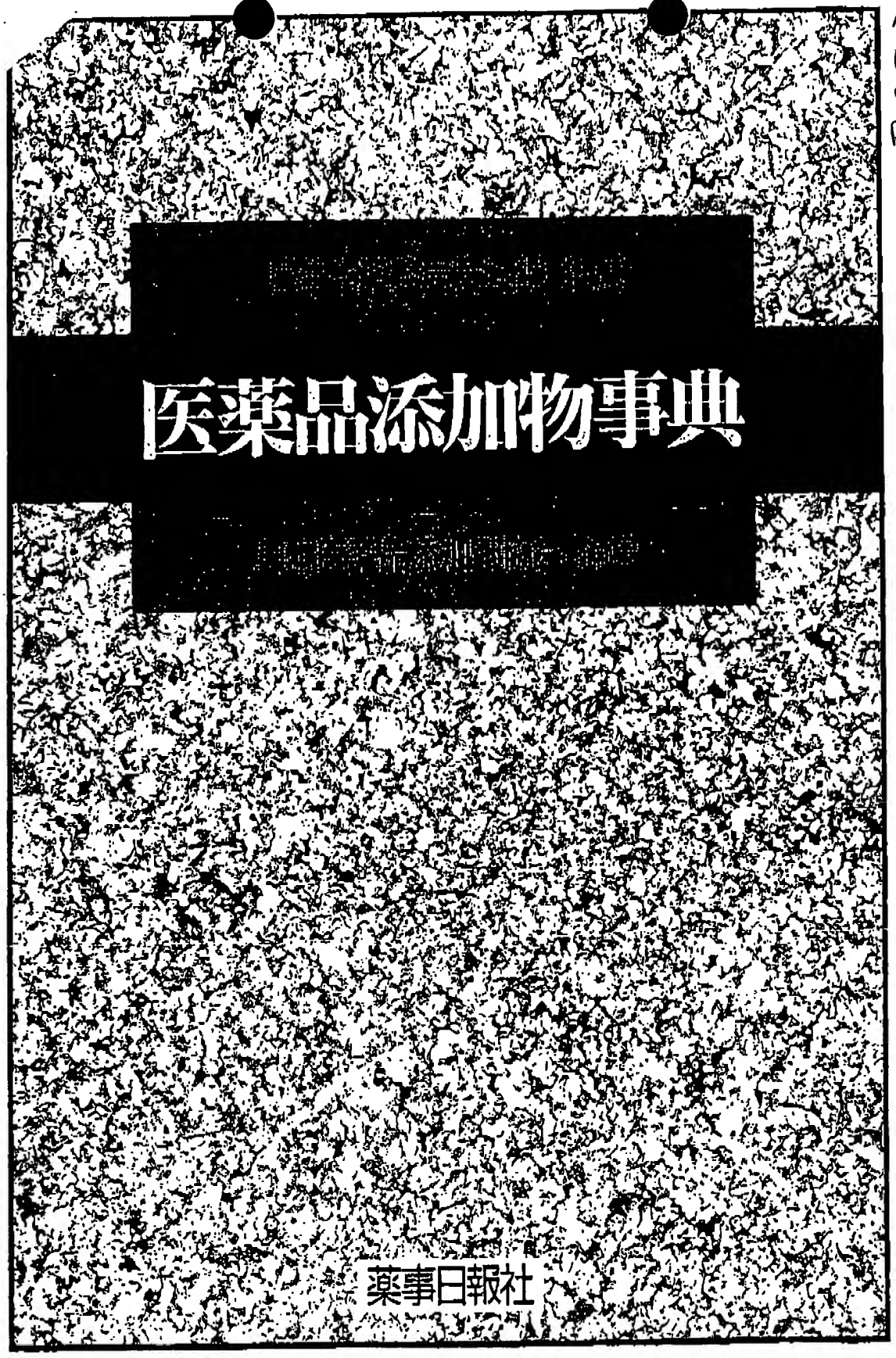
１４．薬効成分又は薬効成分と希釈剤からなる表面改質用粉体を、表面改質基材と混合して表面改質し、直接打錠可能な流動性を有する薬効成分含有表面改質粉体を調製し、次いで崩壊剤を混合して、直接打錠し、請求項１１から１３のいずれかに記載の速崩壊型錠剤を製造する、速崩壊型錠剤の製造方法。

１５．請求項１から９のいずれかに記載の薬効成分含有表面改質粉体を、必要に応じて添加剤と混合し、直接打錠して錠剤を製造するための、該薬効成分含有表面改質粉体の使用。

１６．速崩壊型錠剤を製造するための請求項１５記載の使用。

１７．請求項１から９のいずれかに記載の薬効成分含有表面改質粉体を、必要に応じて添加剤と混合し、直接打錠して錠剤を製造する、製剤の製造方法。

１８．薬効成分含有表面改質粉体を崩壊剤と混合して速崩壊型錠剤を製造する、請求項１７記載の製造方法。



Japanese Pharmaceutical Excipients

APPENDIX A
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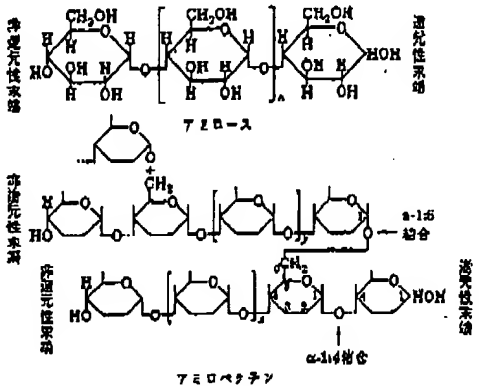
部分アルファー化デンプン

108906

【英名】 Partly Pregelatinized Starch

【別名】 アルファー化デンプン(100418)，加工デンプン (109965)，PCS

【構造】



【参考文献】 薬添規

【概要】 白色～帯黄白色の粉末．トウモロコシデンプンを水と共に常圧下又は加圧下で加熱して，でんぷん粒を部分的にアルファー化して乾燥したもの．水を加えると膨潤し，白濁した液となる．鏡検するとき，球形又は多角形で，稜角を有しない単粒からなり，しばしば互いに集まって複粒となっている．エタノールにほとんど溶けない．pH4.0～7.0(1g→50ml)．

【参考規格】 塩化物 0.030%以下，重金属 20ppm 以下，ヒ素 2ppm 以下，亜硫酸 0.003%以下．酸化性物質 脱塩内，乾燥減量 13%以下(1g，105°，3時間)，強熱残分 0.5%以下 (2g)．

【貯法】 密閉容器

【用途】 結合剤，賦形剤，崩壊剤

【投与経路・最大使用量】 経口投与 1.2g，一般外用剤 5.3mg

【商品名(メーカー)】 PCS(旭化成工業)，スターチ1500 (日本カラコン (カラコン))

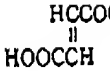
フマル酸

102419

【英名】 Fumaric Acid

【参考文献】 薬添規，食添，外原規，CAS No.110-17-8

【構造】



$C_4H_4O_4$：116.07

【概要】 白色の結晶又は結晶性の粉末．においはなく，特異な酸味．ジメチルホルムアミドに溶けやすく，メタノール又はエタノールにやや溶けやすく，水又はエーテルに溶けにくい．アンモニア試液又は水酸化ナトリウム試液に溶ける．加熱するとき，昇華する．

【参考規格】 含量 (脱水物換算) 99.5%以上．紫外吸収スペクトル 吸収極大波長204～208nm，水(1→200000)．固状 0.5g，水酸化ナトリウム試液10ml，無色澄明．融点：約290°(封管中，分解，105°で3時間乾燥後)．硫酸塩 0.010%以下．重金属 10ppm 以下，ヒ素 2ppm 以下，マレイン酸 0.1%以下 (HPLC)．水分 0.5%以下 (2g)．強熱残分 0.05%以下 (2g)．

【貯法】 密閉容器

【用途】 安定(化)剤，増沢剤，矯味剤，結合剤

【投与経路・最大使用量】 経口投与 50mg，殺虫剤 7mg．

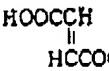
【商品名(メーカー)】 (日本触媒，武田薬品工業，日本油脂，協和発酵工業，三菱化成，田辺製薬，理研化学工業)

フマル酸一ナトリウム

104325

【英名】 Monosodium Fumarate

【構造】



$C_4H_3NaO_4$：138.06

【参考文献】 局外規，食添，CAS No. 141-53-7

【概要】 白色の結晶性の粉末．においはなく，特異な酸味がある．水にやや溶けにくく，メタノール，エタノール又はエーテルにほとんど溶けない．pH3.0～4.0 (1.0g，水30ml)．

【参考規格】 含量 乾燥後，98.0～102.0%．紫外吸収スペクトル 吸収極大波長204～208nm，水 (1→

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